



## General

### Guideline Title

Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965.

### Bibliographic Source(s)

Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, Jewett A, Baack B, Rein DB, Patel N, Alter M, Yartel A, Ward JW, Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. MMWR Recomm Rep. 2012 Aug 17;61(RR-4):1-32. [99 references] [PubMed](#)

### Guideline Status

This is the current release of the guideline.

## Regulatory Alert

### FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [October 4, 2016 – Direct-acting Antivirals](#) : The U.S. Food and Drug Administration (FDA) is warning about the risk of hepatitis B virus (HBV) becoming an active infection again in any patient who has a current or previous infection with HBV and is treated with certain direct-acting antiviral (DAA) medicines for hepatitis C virus. In a few cases, HBV reactivation in patients treated with DAA medicines resulted in serious liver problems or death.

## Recommendations

### Major Recommendations

Definitions for the quality of the evidence (High, Moderate, Low, Very Low) and strength of recommendation (Strong, Weak) are provided at the end of the "Major Recommendations" field.

The following recommendations for hepatitis C virus (HCV) testing are intended to augment the *Recommendations for Prevention and Control of HCV Infection and HCV-Related Chronic Disease* issued by the Centers for Disease Control and Prevention (CDC) in 1998. In addition to testing adults of all ages at risk for HCV infection, CDC recommends that:

- Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk (Strong Recommendation, Moderate Quality of Evidence)
- All persons identified with HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions (Strong Recommendation, Moderate Quality of Evidence)

Providers and patients can discuss HCV testing as part of an individual's preventive health care. For persons identified with HCV infection, CDC recommends that they receive appropriate care, including HCV-directed clinical preventive services (e.g., screening for alcohol use, hepatitis A and hepatitis B vaccination as appropriate, and medical monitoring of disease). Recommendations are available to guide treatment decisions. Treatment decisions should be made by the patient and provider after several factors are considered, including stage of disease, hepatitis C genotype, comorbidities, therapy-related adverse events, and benefits of treatment.

#### Public Health Testing Criteria

HCV testing of persons in the 1945–1965 birth cohort is consistent with established general public health screening criteria as evidenced by the following factors: 1) HCV infection is a substantial health problem that affects a large number of persons, causes negative health outcomes, and can be diagnosed before symptoms appear; 2) testing for HCV infection is readily available, minimally invasive, and reliable; 3) benefits include limiting disease progression and facilitating early access to treatments that can save significant life years; and 4) testing is cost effective. Such testing would help identify unrecognized infections, limit transmission, and help HCV-infected persons receive beneficial care and treatment before onset of severe HCV-related disease.

#### Testing Methods

##### Hepatitis C Antibody Testing

Laboratory testing methods for HCV included in these recommendations were established by CDC's *Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus* in 2003. No new methods are introduced in these recommendations. HCV testing should be initiated with a U. S. Food and Drug Administration (FDA)-approved test for antibody to HCV (anti-HCV). These assays are highly sensitive and specific. An HCV point-of-care assay that can provide results in <1 hour is available for clinical use. An immunocompetent person without risks for HCV infection who tests anti-HCV negative is not HCV-infected and no further testing for HCV is necessary. Additional testing might be needed for persons who have ongoing or recent risks for HCV exposure (e.g., injection-drug use) and persons who are severely immunocompromised (e.g., certain patients with human immunodeficiency virus/acquired immune deficiency syndrome [HIV/AIDS] or those on hemodialysis).

A person whose anti-HCV test is reactive should be considered to either 1) have current HCV infection or 2) have had HCV infection in the past that has subsequently resolved (i.e., cleared). To identify persons with active HCV infection, persons who initially test anti-HCV positive should be tested by an HCV nucleic acid test (NAT).

##### Hepatitis C Nucleic Acid Testing

An FDA-approved HCV nucleic acid test (NAT) (also referred to as an "HCV RNA test") should be used to identify active HCV infection among persons who have tested anti-HCV positive; FDA-approved tests include both quantitative HCV NATs (for HCV viral load) and qualitative NATs (for presence or absence of viremia). Persons who test anti-HCV positive or have indeterminate antibody test results who are also positive by HCV NAT should be considered to have active HCV infection; these persons need referral for further medical evaluation and care. A person who is anti-HCV positive but who tests negative by HCV NAT should be considered to not have active HCV infection.

##### Other HCV-Related Testing Issues

Quantitative NATs assess the level of viremia in the bloodstream expressed as HCV viral load. Although viral load is a critical marker for the effectiveness of treatment, it is not a reliable indicator of stage of disease. Similarly, liver enzyme tests (i.e., alanine aminotransferase [ALT]) reflect the level of liver inflammation at the time of the test, but are not correlated consistently with the stage of liver disease. ALT levels are subject to fluctuations associated with many factors other than infection, including body mass index (BMI) and use of alcohol or medication.

#### Management of Persons Tested for HCV Infection

##### Communicating Test Results to Persons Tested for HCV

##### *Negative Anti-HCV Test Results*

Persons with negative anti-HCV test results should be informed of their test results and reassured that they are not infected unless they were

recently at risk for infection (e.g., current injection-drug use). Repeat testing should be considered for persons with ongoing risk behaviors.

#### *Positive Anti-HCV and Negative HCV Ribonucleic Acid (RNA) Test Results*

Persons who are anti-HCV positive but have an HCV RNA-negative test result should be informed that they do not have HCV infection and do not need follow-up testing.

#### *Positive Anti-HCV and HCV RNA Test Results*

Persons who test positive for both HCV antibody and HCV RNA should be informed that they have HCV infection and need further medical evaluation for liver disease, ongoing medical monitoring, and possible treatment. At the time positive test results are communicated to patients, health-care providers should evaluate the patient's level of alcohol use and provide a brief alcohol intervention if clinically indicated (see "Alcohol-Use Reduction" below). Persons with HCV infection also should be provided information (either through face-to-face sessions, video, or written materials) about 1) HCV infection, 2) risk factors for disease progression, 3) preventive self-care and treatment options, and 4) how to prevent transmission of HCV to others. HCV-infected persons also should be informed about the resources available to them within their communities, including providers of medical evaluation and social support.

#### Post-Test Counseling Messages

Persons infected with HCV can benefit from the following counseling messages.

- Contact a health-care provider (either a primary-care clinician or specialist [e.g., in hepatology, gastroenterology, or infectious disease]) for:
  - Medical evaluation of the presence or development of chronic liver disease
  - Advice on possible treatment options and strategies
  - Advice on how to monitor liver health, even if treatment is not recommended
- Protect the liver from further harm by:
  - Considering hepatitis A and B vaccination if susceptible and if liver disease is present
  - Reducing or discontinuing alcohol consumption
  - Avoiding new medicines, including over-the-counter and herbal agents without first checking with their health-care provider
  - Obtaining HIV risk assessment and testing
- For persons who are overweight (BMI  $\geq 25\text{kg/m}^2$ ) or obese (BMI  $\geq 30\text{kg/m}^2$ ):
  - Consider weight management or losing weight
  - Follow a healthy diet and stay physically active
- To minimize the risk for transmission to others:
  - Do not donate blood, tissue, or semen
  - Do not share appliances that might come into contact with blood, such as toothbrushes, dental appliances, razors, and nail clippers

#### Alcohol-Use Reduction

Messages to decrease alcohol use should be provided to persons infected with HCV. Alcohol screening and brief interventions (SBI) for referral for treatment can reduce the number of drinks consumed per week and episodes of binge drinking. SBI includes screening patients for excessive alcohol consumption, brief counseling for those who screen positive, and referral to specialized alcohol treatment for patients with possible alcohol dependence. The brief intervention is also an opportunity to communicate the HCV-associated risks posed by alcohol consumption and provide options for behavioral change. The U.S. Preventive Services Task Force (USPSTF) recommends screening and behavioral counseling interventions to reduce alcohol misuse by adults in primary-care settings. Screening tools shown to be effective in eliciting a history of alcohol use from patients include the Alcohol Use Disorders Identification Test (AUDIT). Screening tools are available from the [National Institute on Alcohol Abuse and Alcoholism](#) [redacted], and [World Health Organization \(WHO\)](#) [redacted] has published intervention tools to help patients adopt healthy behaviors regarding alcohol use.

#### Linkage to Care and Treatment

Many persons identified as HCV-infected do not receive recommended medical evaluation and care after the diagnosis of HCV infection; this gap in linkage to care can be attributed to several factors, including being uninsured or underinsured, failure of providers to provide a referral, failure of patients to follow up on a referral, drug or alcohol use, and other barriers. The lack of such care, or substantial delays before care is received, negatively impacts the health outcomes of infected persons. Routine testing of persons born during 1945–1965 is expected to lead to more HCV-infected persons being identified earlier in the course of disease. However, to improve health outcomes, persons testing positive for HCV must be provided with appropriate care and treatment. Linking patients to care and treatment is a critical component of the strategy to reduce the burden of disease.

Strategies are needed for HCV-infected persons who are experiencing barriers to care. These persons might benefit from the replication of effective linkage-to-care models and the development of other evidence-based interventions. Active linkage-to-care programs provided in a culturally sensitive manner (e.g., the use of case managers to schedule appointments, bring infected patients to doctors' appointments, and follow-up with patients) have been found to be more effective than passive referral methods (e.g., providing patients with information about the disease and a list of resources or referrals to medical care). Such linkage creates opportunities for patients to receive information, vaccinations, and prevention counseling messages and to more fully engage in care. Once patients receive care, case management can provide active linkage to social services, referral to substance abuse services, and assistance with transportation and housing. Recommendations for the medical management of HCV infection and disease are updated regularly by the American Association for the Study of Liver Diseases (AASLD).

Notable advances are being made in the care, management, and treatment of HCV infection at the time of publication of this recommendation. Although primary care clinicians can readily provide much of the care necessary for initial evaluation and management of persons with HCV infection, antiviral treatment is complex, and collaboration between primary-care providers and specialists facilitates delivery of optimal care. CDC is working with academic and clinical partners and with other federal and state agencies to replicate best practices and develop new models for HCV care.

#### Definitions:

#### Quality of Evidence

The quality of the evidence was categorized as being "high," "moderate," "low," or "very low" depending on the established criteria for rating the quality up or down. The quality of evidence for each of the outcomes was rated down if it met at least one of the following five criteria: 1) risk of bias; 2) inconsistency or heterogeneity; 3) indirectness (addressing a different population than the one under consideration); 4) imprecision; or 5) publication bias. Conversely, the quality of the evidence was rated up if it met any of three criteria: 1) large effect size; 2) dose-response; or 3) plausible residual confounders (i.e., when biases from a study might be affecting the estimated apparent intervention effect).

#### Strength of Recommendation

The following four factors are considered when determining the relevance and strength of a Grading of Recommendations Assessment, Development, and Evaluation (GRADE)-based recommendation: 1) quality of evidence, 2) balance between benefits and harms, 3) values and preferences, and 4) resource implications. During the consultation, the Work Group considered each of these factors in light of the evidence presented. A statement based on the direction and strength of the recommendation was developed using the GRADE criteria; statements were either "for" or "against" an intervention and were either strong (designated by a "should" statement) or conditional (designated by a "may consider" statement).

## Clinical Algorithm(s)

None provided

## Scope

## Disease/Condition(s)

Hepatitis C virus (HCV) infection

## Guideline Category

Counseling

Diagnosis

Evaluation

Management

Prevention

Screening

Treatment

## Clinical Specialty

Family Practice

Gastroenterology

Infectious Diseases

Internal Medicine

Preventive Medicine

## Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

Substance Use Disorders Treatment Providers

## Guideline Objective(s)

- To provide birth-year-based recommendations which are intended to augment, not replace, the 1998 hepatitis C virus (HCV) testing guidelines
- To define an additional target population for HCV testing
- To recommend clinical preventive services, regular medical monitoring, and behavioral changes for those affected by HCV
- To discuss early identification, linkage to care, and clinical evaluation for persons with HCV

## Target Population

Persons in the United States born between 1945-1965

## Interventions and Practices Considered

1. One-time testing for hepatitis C virus (HCV) without prior ascertainment of HCV risk
2. Brief alcohol screening and intervention as clinically indicated
3. Referral to appropriate care and treatment services for HCV infection and related conditions

## Major Outcomes Considered

- All-cause mortality
- Hepatocellular carcinoma (HCC)
- Sustained virologic response (SVR) (a marker of virologic cure)

- Serious adverse events (SAEs) (i.e., treatment-related side effects)
- Quality of life (QoL)
- Hepatitis C virus (HCV) transmission
- Alcohol brief interventions

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

### Description of Methods Used to Collect/Select the Evidence

#### Literature Review

The Division of Viral Hepatitis (DVH) Steering Committee reviewed current hepatitis C virus (HCV) testing guidelines and existing scientific evidence; systematic reviews and meta-analyses were conducted to synthesize the evidence available for the review questions. This evidence was compiled and presented to the Work Group throughout the development process.

The systematic review process for these recommendations was separated into two stages: 1) a review of HCV infection prevalence to determine the effect of a birth-year testing strategy, and 2) a review of the effects of testing persons born during 1945–1965 on patient-important outcomes. Search strategies varied for each stage; however, following the initial collection of results from the search, titles and abstracts were reviewed by two persons. If disagreement on the inclusion of an article occurred, an independent third reviewer decided whether the article would be included. For the titles and abstracts that met the inclusion criteria, the full article was retrieved and reviewed. Information from the full articles was extracted for the Grading of Recommendations, Assessments, Development and Evaluation (GRADE) profiles to conduct the meta-analyses.

#### Prevalence Data

The review of prevalence data was conducted to identify literature addressing a birth-year-based strategy or providing additional support for the prevalence estimates (see Selection of a Target Birth Cohort). The DVH Steering Committee reviewed all literature regarding the effect of a birth-year-based testing strategy for HCV infection that had been considered and published after Centers for Disease Control and Prevention's (CDC) 1998 recommendation. To be selected for review, articles had to have been published during 1995–2011, describe results of U.S.-based studies, and include participants within the target population (i.e., the 1945–1965 birth cohort). Case studies and studies of persons co-infected with hepatitis B virus (HBV) or human immunodeficiency virus (HIV) were excluded. Six databases were searched for primary research, including grey literature and conference abstracts: MEDLINE, EMBASE, Sociological Abstracts, Cochrane Library (e.g., Database of Systematic Reviews, Central Register of Controlled Trials, and Economic Evaluation Database), CINAHL, and Database of Abstracts of Reviews of Effects (DARE) (see Appendix D of original guideline document).

#### Patient-Important Outcomes

A literature search for the effect of HCV testing and treatment on patient-important outcomes was conducted (see Appendix E of original guideline document). A search of previously published systematic reviews and meta-analyses was conducted initially and used to address the patient-important outcomes when available and of high quality. When systematic reviews or meta-analyses were unavailable, primary studies were sought and added to the results. When possible, data from primary studies were entered into systematic review software (Review Manager, 2008) to produce meta-analyses for estimation of effect sizes. Otherwise, effect size data were extracted directly from published meta-analyses.

Separate, targeted literature reviews were conducted for those outcomes considered important or critical to decision making (i.e., given a GRADE rating of  $\geq 4$ ); these outcomes included:

- All-cause mortality

- Hepatocellular carcinoma (HCC)
- Sustained virologic response (SVR) (a marker of virologic cure)
- Serious adverse events (SAEs) (i.e., treatment-related side effects)
- Quality of life (QoL)
- HCV transmission
- Brief alcohol interventions

Systematic reviews for all-cause mortality, SVR, SAEs, QoL, HCV, and brief alcohol interventions were conducted for literature published in MEDLINE from 1995 through July 2011. For HCC, a comprehensive search for HCC was conducted for literature published during 1946–2011 in MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, CINAHL, Web of Science, and DARE.

The selection criteria for the primary literature search included intervention studies (i.e., controlled trials, cohort studies, and case-control studies) conducted worldwide and published in English. Case studies were excluded, along with studies of transplant recipients and persons co-infected with HBV or HIV, if they were not controlled for in the analysis. To be selected, studies needed to present data inclusive of persons born during 1945–1965. Because DAAs have only recently been licensed, evidence was insufficient on their long-term effect on the patient-important outcomes. Therefore, only studies providing treatment regimens with pegylated interferon (with and without ribavirin) or interferon (with or without ribavirin) were examined.

A systematic, targeted review was conducted to examine potential harmful and beneficial patient-important outcomes associated with HCV testing and treatment. A similar review also was conducted to examine reduction or cessation of alcohol use associated with brief interventions provided to persons identified as HCV-infected. Only those outcomes considered critical to decision making (i.e., all-cause mortality, HCC, SVR, treatment-related SAEs, QoL, HCV transmission, and alcohol use) were graded on their quality and used to inform the strength of the recommendations.

## Number of Source Documents

- For hepatitis C virus prevalence, 31 eligible study reports were identified after full-text screening.
- For all-cause mortality data, 1 eligible study report was identified after full-text screening.
- For hepatocellular carcinoma, 30 full-text articles were identified.

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

Quality of Evidence

The quality of the evidence was categorized as being "high," "moderate," "low," or "very low" depending on the established criteria for rating the quality up or down. The quality of evidence for each of the outcomes was rated down if it met at least one of the following five criteria: 1) risk of bias; 2) inconsistency or heterogeneity; 3) indirectness (addressing a different population than the one under consideration); 4) imprecision; or 5) publication bias. Conversely, the quality of the evidence was rated up if it met any of three criteria: 1) large effect size; 2) dose-response; or 3) plausible residual confounders (i.e., when biases from a study might be affecting the estimated apparent intervention effect).

## Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

These recommendations were developed using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology, which has been adopted by approximately 60 organizations, including the Centers for Disease Control and Prevention (CDC) federal advisory committees (i.e., the Advisory Committee on Immunization Practices and the Healthcare Infection Control Practices Advisory Committee), the World Health Organization, Infectious Diseases Society of America (IDSA), American Gastroenterological Association (AGA), and the Cochrane Collaboration ([www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)). GRADE provides guidance and tools to define research questions, develop an analytic framework, conduct systematic reviews, assess the overall quality of the evidence, and determine the direction and strength of the recommendations.

Research questions were formulated to guide the development of the recommendations using a population, intervention, comparator, and outcome (PICO) format. The research questions were developed to support a two-stage approach to the evidence review: 1) determine the baseline prevalence of hepatitis C virus (HCV) infection and 2) measure the effects of an intervention (i.e., patient-important benefits and harms).

Per the GRADE process, the HCV Birth Cohort Testing Work Group designed an analytic framework (see Appendix C of the original guideline document), which was used to examine patient-important outcomes associated with each step of the testing effort, from the identification of the target population to the treatment of persons found to be infected with HCV. To measure the benefits and harms of HCV screening and treatment, patient-important outcomes were compiled. These outcomes were ranked, each according to its relevance to the recommendation (a rating of 1–3 being of low importance; 4–6 being important but not critical to decision making; and 7–9 as critical to decision making). Literature reviews were conducted on outcomes identified as important or critical to decision making. Work Group members had three opportunities to rank the outcomes: 1) when the outcomes were first identified, 2) after the evidence was presented, and 3) during the discussion of the benefits and harms, allowing the Work Group to weigh the relative importance of the outcomes based on the evidence presented and the benefits and harms.

The quality of the evidence for each patient-important outcome was assessed collectively by individual outcome, not by individual studies, in the GRADE profiler software (GRADEpro 3.6). See "Rating Scheme for the Strength of the Evidence" field.

## Research Questions

To facilitate a succinct, systematic review of the evidence, the Work Group developed the following review questions to be considered when examining prevalence data and patient-important outcomes:

- What is the effect of a birth-year based testing strategy versus the standard of care (i.e., risk-based testing) for identification of HCV infection?
- Should HCV testing (versus no testing) be conducted among adults at average risk for infection who were born during 1945–1965?
- Among persons tested and identified with HCV infection, is treatment-related sustained virologic response (SVR) (versus treatment failure) associated with reduced liver-related morbidity and all-cause mortality?
- Should HCV testing followed by brief alcohol interventions (versus no intervention) be carried out to reduce or cease drinking among HCV-infected persons?

Review questions were aligned with the analytic framework and were formed in accordance with PICO. The division of these questions into two topics, prevalence data and patient-important outcomes, reflects the two-stage approach that was used to 1) define the testing strategy and birth years of interest, and 2) examine the effects of testing persons born during 1945–1965 for HCV infection. Because the patient-important outcomes questions encompass many outcomes, they are formed without listing one specific outcome; they present only the population, intervention, and comparator.

## Methods Used to Formulate the Recommendations

### Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Centers for Disease Control and Prevention (CDC) employed the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology to inform the guideline development process. In April 2011, CDC convened the hepatitis C virus (HCV) Birth Cohort Testing Work Group to explore the practicality of developing a recommendation for one-time HCV testing for persons unaware of their infection status. Epidemiologic data exist to support the consideration of a birth year testing strategy; however, the GRADE process dictated that a formal review of the literature be conducted to examine the effect that this testing would have on diagnosing persons unaware of their HCV infection status, as well as the potential benefits and harms that this strategy would have on persons tested.



The Work Group consisted of 1) a steering committee within CDC's Division of Viral Hepatitis (DVH), which led and conducted the evidence reviews; 2) representatives from DVH's Laboratory, Prevention, and Epidemiology and Surveillance Branches, who were tasked with reviewing and providing input on the evidence compiled by the steering committee through biweekly meetings; and 3) external (to CDC) representatives, who provided input on materials compiled by the steering committee through teleconferences, an evidence grading methodology training workshop, and a consultation. External representatives were selected on the basis of expertise with viral hepatitis; members included representatives from hepatitis C-related community-based organizations, persons living with HCV infection, hepatologists, economists, infectious disease specialists, and guideline methodologists. A wide range of disciplines, organizations, and geographic regions was represented, to include:

- Federal organizations (Agency for Healthcare Research and Quality, National Cancer Institute, Food and Drug Administration, Veteran's Affairs, Health Resources and Services Administration, Substance Abuse and Mental Health Services Administration, and National Institute of Diabetes Digestive and Kidney Diseases)
- Professional associations (American Medical Association, American College of Physicians, American Academy of Family Physicians, Association of Public Health Laboratories, and Council of State and Territorial Epidemiologists)
- Community-based organizations (Adult Viral Hepatitis Prevention Coordinator Program, National Viral Hepatitis Roundtable, CopeHealth, National Association of State and Territorial AIDS Directors, and Hepatitis Education Project)
- Organizations of medical specialists who frequently see patients in consultation or referral (American Association for the Study of Liver Diseases [AASLD], American Gastroenterological Association [AGA], and Infectious Diseases Society of America [IDSA])
- Several subject matter experts (e.g., hepatologists, economists, infectious disease specialists, and guideline methodologists) also served as members of the external group

Several subject matter experts (e.g., hepatologists, economists, infectious disease specialists, and guideline methodologists) also served as members of the external group.

Comprehensive systematic reviews of the literature were conducted, analyzed, and assessed in two stages to examine the availability and quality of the evidence regarding HCV infection prevalence and the health benefits and harms associated with one-time HCV testing for persons unaware of their status.

Work Group members communicated through teleconferences and attended an in-person workshop on GRADE methodology. Initial evidence from the systematic review of the prevalence data was shared during the teleconferences, and the target birth years were selected. Following that selection, the systematic review focused on the HCV-associated morbidity and mortality that might be altered by a recommendation for one-time testing of persons born during 1945–1965.

In August 2011, CDC convened a 2-day consultation with Work Group members to 1) review and evaluate the quality of the evidence for the proposed birth cohort-based strategy, 2) consider benefits versus harms of patient-important outcomes, 3) weigh the variability between the values and preferences of HCV testing among potential patients, and 4) consider resource implications. During the consultation, a summary of findings table addressing each patient-important outcome was presented to consultation attendees for discussion (see Appendix B of original guideline document). Work Group members later provided input on the quality of the evidence and strength of the recommendations. Following the consultation, the DVH Steering Committee and other DVH representatives reviewed the information and reached a decision regarding the strength of the recommendations. At that time, a recommendations statement and qualifying remarks were developed in accordance with GRADE methodology.

## Rating Scheme for the Strength of the Recommendations

The following four factors are considered when determining the relevance and strength of a GRADE (Grading of Recommendations Assessment, Development and Evaluation)-based recommendation: 1) quality of evidence, 2) balance between benefits and harms, 3) values and preferences, and 4) resource implications. During the consultation, the Work Group considered each of these factors in light of the evidence presented. A statement based on the direction and strength of the recommendation was developed using the GRADE criteria; statements were either "for" or "against" an intervention and were either strong (designated by a "should" statement) or conditional (designated by a "may consider" statement).

## Cost Analysis

When examining the possibility of including persons born during 1966–1970 with the target population (i.e., 1945–1965 cohort), it was determined that such a strategy would direct testing to approximately 20 million additional persons at a cost of approximately \$1.08 billion, resulting in identification of an additional 300,000 persons with chronic infection. The number needed to screen to avert a single hepatitis C virus (HCV)-related death was lower in the 1945–1965 birth cohort compared with the 1945–1970 birth cohort (607 and 679, respectively). Data

collected through a series of 12 consumer focus groups in three different U.S. cities demonstrated that the 1945–1965 birth cohort is a recognized subpopulation known as the baby boomers; familiarity with this subpopulation and the term used to describe it likely will facilitate adoption of the recommendation. On the basis of these assessments, Centers for Disease Control and Prevention (CDC) selected the 1945–1965 birth cohort as the target population.

## Resource Implications

Only two U.S.-based studies specifically examined the cost effectiveness and resource implications of birth-year-based HCV testing linked to HCV care and treatment; both studies found the interventions to be cost effective. These studies, which evaluated slightly different definitions of birth cohort, compared birth-cohort testing and treatment with the status quo of risk- and medical indication-based testing recommendations; both studies demonstrated nearly identical cost-effectiveness results. The first study, which defined the birth cohort as persons born during 1945–1965, estimated a cost per quality-adjusted life year (QALY) gained of \$35,700 on the basis of a 12-week, response-guided course of telaprevir and pegylated interferon plus ribavirin (PR); cost per QALY was an estimated \$15,700 when assuming treatment with PR alone. The second study defined the birth cohort as persons born during 1946–1970 and estimated a cost per QALY gained of \$39,963 for patients treated with telaprevir in addition to PR. Both modeling studies assumed that liver disease progression would not continue for those who achieve sustained virologic response (SVR).

These cost-effectiveness studies had different assumptions about the timing of HCV testing and treatment. The study that examined the 1945–1965 birth cohort included all possible costs and benefits in a single year, whereas the study that examined the 1946–1970 birth cohort assumed 20% of the eligible population would be screened and treated each year for 5 years. Testing costs (including antibody testing, nucleic acid testing of antibody positives, and posttest counseling) were estimated at \$54 per person tested.

The birth-cohort testing strategy will reduce morbidity and mortality (see Table 3 of original guideline document), saving future HCV-related medical expenditures. However, in the immediate future, the increase in testing and treatment of persons born during 1945–1965 will cost more than that associated with current risk-based testing and treatment strategies. Several factors contribute to projected increases in treatment costs, including an expected increase in the number of persons tested and treated for HCV and the higher costs associated with combination PR/direct-acting antiviral agents (DAA) therapy versus PR alone (see Table 4 of original guideline document). Costs can be compared using four different scenarios: risk-based testing with PR therapy; risk-based testing with PR therapy and DAA; birth cohort testing with PR therapy; and birth-cohort testing with PR therapy and DAA, the current standard of care (see Table 4 of original guideline document).

To inform cost projections for the birth cohort HCV testing strategy, colorectal screening rates were reviewed to estimate the testing costs associated with one-time HCV testing for persons in the 1945–1965 birth cohort. Both interventions focus on screening at a single time point in time (i.e., at age 50 years for colorectal screening); therefore, data from colorectal screening programs are useful for estimating the rate of adoption of a recommendation for one-time prevention services. In an analysis of 2005 National Health Interview Survey data (a nationally representative household survey), 19.8% of women and 23.7% of men reported receiving colorectal screening during the preceding 3 years (the time since implementation of the United States Preventive Service Task Force [USPSTF] screening recommendation). These percentages were obtained after years of updated colorectal screening recommendations and implementation of educational campaigns, so they likely are higher than those expected to follow adoption of HCV testing recommendations. However, adopting the birth-cohort recommendations at the same level would result in testing approximately 5.6 million women and 6.7 million men for HCV within the first 3 years of implementation, at a cost of \$664 million; approximately 400,000 persons with HCV infection would be identified.

See Table 4 of original guideline document: Selected Medical Cost, by HCV Testing and Treatment Strategy—United States, 2012.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

Following the evidence review, the Centers for Disease Control and Prevention's (CDC) Division of Viral Hepatitis (DVH) developed this report, which was then peer-reviewed by external experts and posted for public comment. CDC reviewed and considered all public comments in developing the final recommendations.

Feedback from the public was solicited through conference presentations, meetings with national stakeholders, and public comment. Further, the

proposed guidelines were peer-reviewed by external experts in viral hepatitis. A Federal Register notice was released on May 18, 2012, announcing the availability of the draft recommendations for public comment through June 8, 2012. In addition, external Work Group members were asked to comment on the recommendations statement and remarks during the public comment process. Feedback from the public comment period was reviewed by the DVH Steering Committee, and the draft was modified accordingly. Throughout the development process, CDC also sought input from participants at national conferences, including the American Association for the Study of Liver Diseases (AASLD) 2011 Single Topic Conference, the 2010 Annual Meeting of the American Public Health Association, the 2010 AASLD Conference, the 2011 Guidelines International Network Conference, and Digestive Disease Week 2012.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is specifically stated for selected recommendations (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Clinical preventive services, regular medical monitoring, and behavioral changes can improve health outcomes for persons with hepatitis C virus (HCV) infection. As HCV-associated liver disease progresses, the likelihood of sustaining a treatment response decreases; therefore, early identification, linkage to care, and clinical evaluation are critical disease prevention interventions.
- With the advent of new therapies that can halt disease progression and provide a virologic cure (i.e., sustained viral clearance following completion of treatment) in most persons, targeted testing and linkage to care for infected persons in this birth cohort is expected to reduce HCV-related morbidity and mortality.

### Potential Harms

- Adverse events of drug treatments
- Complications associated with liver biopsy such as pain, bleeding, intestinal perforation, and death
- Harms (worry, anxiety, concern about insurability) associated with the receipt of false-positive test result, the need to wait or return for test results, access to treatment, and the effect of hepatitis C virus (HCV)-infection notification on insurance and employment

## Qualifying Statements

### Qualifying Statements

- These recommendations do not replace previous guidelines for Hepatitis C virus (HCV) testing that are based on known risk factors and clinical indications. Rather, they define an additional target population for testing: persons born during 1945–1965. CDC developed these recommendations with the assistance of a work group representing diverse expertise and perspectives. The recommendations are informed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, an approach that provides guidance and tools to define the research questions, conduct the systematic review, assess the overall quality of the evidence, and determine strength of the recommendations. This report is intended to serve as a resource for health-care professionals, public health officials, and organizations involved in the development, implementation, and evaluation of prevention and clinical services. These recommendations will be reviewed every 5 years and updated to include advances in the published evidence.
- Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.
- References to non-Centers for Disease Control and Prevention (CDC) sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

Living with Illness

Staying Healthy

### IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, Jewett A, Baack B, Rein DB, Patel N, Alter M, Yartel A, Ward JW, Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. *MMWR Recomm Rep*. 2012 Aug 17;61(RR-4):1-32. [99 references] [PubMed](#)

### Adaptation

Not applicable: This guideline was not adapted from another source.

### Date Released

2012 Aug 17

## Guideline Developer(s)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

## Source(s) of Funding

United States Government

## Guideline Committee

Hepatitis C virus (HCV) Birth Cohort Testing Work Group

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## Financial Disclosures/Conflicts of Interest

Work Group participants were required to disclose conflicts of interest and were notified of the restrictions regarding lobbying during the recommendation development process (see Appendix A of original guideline document). No members' activities were restricted based on the information disclosed.

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## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available from the [Centers for Disease Control and Prevention \(CDC\) Web site](#) .

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238 .

## Availability of Companion Documents

The following is available:

- Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Ward JW. Hepatitis C virus testing of persons born during 1945 to 1965: recommendations from the Centers for Disease Control and Prevention. Ann Intern Med 2012 Nov 6;157 (9):1-7. Electronic copies: Available in Portable Document Format (PDF) from the [Annals of Internal Medicine Web site](#) .

In addition, a Continuing Education Examination available at the [Centers for Disease Control and Prevention \(CDC\) Web site](#) .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on October 8, 2012. This summary was updated by ECRI Institute on October 20, 2016 following the U.S. Food and Drug Administration advisory on Direct-acting Antivirals.

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